

such applications is shadowed by the lack of reliable information on their fundamental interaction mechanisms with biological systems. This entails not only specific atomistic interaction mechanisms between individual molecules but also transformation and non-covalent functionalization of the nanoparticles used within a biological organism. For interactions between nanoparticles and RNA or DNA, interference with their regular functioning or induction of damage by, e.g. photocleavage, may offer new routes for biomedical engineering - but potentially also for a number of unwanted effects in cells and bacteria.

We have used atomistic molecular dynamics simulations to study the interaction of polyhydroxylated fullerenes C₆₀(OH)₂₀, i.e. fullerols, with nucleic acids ssRNA, ssDNA and dsDNA. The nucleic acids are modeled by oligomers of 20 arbitrary nucleotide (bp) sequences. The modeling provides atomic-scale information on the binding modes of the fullerols, as well as local structural deformation of nucleic acids by the fullerol binding. The data obtained from the simulations is compared to spectroscopic measurements on solutions containing such nucleic acids and fullerols.

[1] T. Da Ros and M. Prato, Chem. Commun., 1999, 663-669.

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A Microdevice To Indicate Human Neural Stem Cell Differentiation Potential

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"Stem cells" is a term used to describe primal cells capable of differentiating into a number of specialised cell types. Stem cells have potential importance for a range of clinical and cell-based therapies. However, major difficulties lie in identifying these stem cells from differentiated offspring due to lack of appropriate biomarkers.

Dielectrophoresis (DEP) is a non-invasive technique utilizing the induced motion of particles in non-uniform electric fields. Particles experiencing such forces can be made to exhibit a variety of motions including attraction to, and repulsion from, regions of high electric field by changing the frequency of the applied electric field. The main factors influencing the electrical properties of a cell are the surface charge, the membrane capacitance and the conductivity of the cytoplasm which combine to form an electrophysiological "fingerprint" of the cell.

Human neural stem cells (HuNSCs) are of interest because of their potential use for treatment of central nervous system injuries and disease. In this study we investigated two types of HuNSCs, which differ in their ability to generate neurons and glia, using DEP in a microdevice system. We have determined the relative contributions of the cells' membrane and cytoplasmic compartments to their overall behaviour in DEP. The results showed that there are significant identifiable differences in the specific capacitance of the membranes of both types of HuNSCs. Furthermore, we have found that the electrophysiological properties of the HuNSC populations changed over time, which correlated with the changing differentiation potential of the cells.

The work demonstrated a novel, label-free technique that predicted the neurogenic potential of HuNSCs by means of detecting differences in the membrane compartment between neurogenic and gliogenic human NSCs.

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A Spectroscopic Monitoring Module Based on a Ceramic Microfluidic Platform

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A 3-dimensional mesofluidic biological monitoring module has been successfully designed and fabricated using a low-temperature co-fired-ceramic

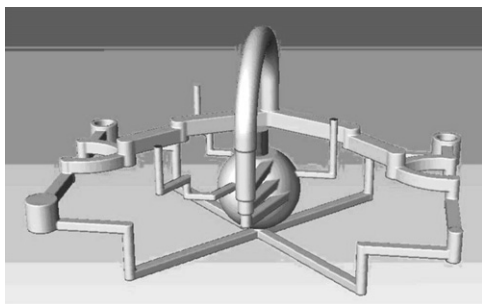


Fig. 1. Scheme of the monitoring module

(LTCC) technology. This mesofluidic device consists of a network of microchannels and a spherical mixing cavity. The selection of appropriate commercially available ceramic tapes has been done with regard to their biocompatibility performance. Specific processing procedures required for the realization of such complex structure are demonstrated. Three dimensional numerical flow simulations have been conducted to characterize the concentration profiles of liquids at a specific measuring port and verified by experiment. The module was successfully applied to study complex chemical reaction kinetics complemented by mathematical modelling.

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Dynamics of Calcitriol Uptake and Signaling using Conjugated Quantum Dots

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Properties exhibited by Semiconductor Nanoparticles (Quantum Dots, (QDs)) make them powerful tools for the use as fluorescent probes for real time imaging. They are characterized by enhanced photostability, and high quantum efficiency compared to conventional organic dyes. Calcitriol, the active form of VitaminD₃, belongs to the group of steroid hormones. Past research lacked to develop active Calcitriol conjugates that are stable over an extended period of time to follow its cellular uptake and intracellular dynamics. In order to design an active conjugate only one hydroxy group within the structure of Calcitriol can be used for coupling to the QD. We successfully developed a bioactive Calcitriol-QD conjugate and imaged the uptake and the dynamics of Calcitriol into cells in real time. Our data show that it is stable for at least 48h at RT. We determined its interaction with the cell membrane and accumulation in the cell nucleus. VitaminD₃ can have both preventive and therapeutic effects by controlling cell growth, the cell cycle, apoptosis, and differentiation - a role greater than earlier views that focused on bone health and maintenance of calcium homeostasis. Epidemiological studies have found a significant association between low serum levels and low dietary intake of VitaminD₃ and the incidence, degree of malignancy, metastases, and mortality of cancers of the breast, prostate, colon, and ovaries. VitaminD₃ when bound to its receptor appears to have significant protective effects against the development of cancer. Based on this research, it has been proposed that taking VitaminD₃ could lower the cancer risk by 50% in colon cancer, and by 30% in breast and ovarian cancer. The mechanism for VitaminD₃'s chemoprevention is not well-defined, but understanding how it works would provide vital information for targeting populations at high risk for developing hormone-dependent cancers.

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The Role of Electrostatics in Sequence Dependent Nucleosome Stability Analysis

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Nucleosome stability is strongly sequence dependent; yet the conformation of the DNA in the nucleosome is sequence independent. The nucleosome conformation is determined only by the histone octamer, and there is an energy penalty for deforming free DNA into this conformation. By comparing all atom molecular models and coarse grained elastic rod based models to experimentally determined free energies, we demonstrate that the contributions to the free energy of nucleosome formation arise from two sources: electrostatics and the local material properties of DNA.

The primary contribution to electrostatic energy in the nucleosome comes from the highly charged yet conserved phosphate backbone of DNA. Since all DNA sequences assume the same conformation in the nucleosome the electrostatic energy associated with the nucleosome conformation of DNA is largely sequence invariant. Thus the electrostatic energy contribution to nucleosome stability is defined not by the conformation of DNA in the nucleosome but by the conformation of free DNA. The free conformation rather than the bound conformation determines the binding free energy.

The material properties of DNA (elastic and van der Waals energies) behave quite differently. These energies are strongly dependent upon the sequence and conformation of the DNA. The conformation of free DNA tends to minimize these energies. When DNA binds the histone octamer and assumes the nucleosomal DNA conformation, the elastic and van der Waals energies associated with such deformation are also strongly sequence dependent. If the DNA sequence possesses intrinsic conformational properties that match those of the nucleosome or if the sequence is suitably flexible then the energy penalty is lower than for sequences which do not possess such characteristics. Both the free and bound states contribute to binding free energy.